AF

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appellant:	Stoughton *et al.*
Serial No.:	09/038,894
Conf. No.:	8909
Cust. No.:	20985
Filed:	March 11, 1998
For:	*METHODS OF DIAGNOSIS AND TRIAGE USING CELL ACTIVATION MEASURES*
Art Unit:	1654
Examiner:	Meller, M.

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03/24/2005
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Stephanie Seidman

REPLY BRIEF ON APPEAL

This Reply Brief is responsive to the Examiner's Answer, mailed on January 24, 2005. Consideration and entry of the remarks below are respectfully requested. A check for the fee to preserve the right for an oral hearing accompanies this Reply Brief.

(1) Grouping of the claims

The Examiner urges that because Appellant allegedly failed to make a statement under 37 C.F.R. §1.197(c)(7) that the claims stand or fail together. Appellant respectfully disagrees.

It is respectfully submitted that this Appeal Brief was filed after September 13, 2004, and is under the new rules and in particular, in accord with rule 37 C.F.R. §41.37. Hence 37 C.F.R. §1.197(c)(7) does not apply. The rule relied upon by the Examiner has been replaced by the new rules that require Appellant to argue the claims separately for separate consideration. It is respectfully submitted that Appellant has argued each of the claims separately in the Appeal Brief. Therefore in compliance with rule 37 C.F.R. §41.37, the claims do not stand or fall together.

(2) Issues

Withdrawal of the rejections under 35 U.S.C. §112 in part and under 35 U.S.C. §103(a) is acknowledged. The remarks below address the outstanding rejections, which are as follows:

(i) Claims 32-36, 38, 41 and 42 are rejected under 35 U.S.C. §112, first paragraph, because the specification allegedly is not enabling for prevention of disease.

(ii) Claims 10-18, 32-36, 38, 41 and 42 are rejected under 35 U.S.C. §112, first paragraph, as being broader than the enabling disclosure. It is alleged that the specification fails to provide enablement for any and all activation lowering therapies and any and all diseases or conditions and any and all methods of assessing cellular activation.

(iii) Claims 10-18, 32-36, 38, 41 and 42 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite in the recitation of "administering activation lowering therapy" and "preventing a disease or disorder."

(3) The claimed methods

As an aid to understanding Appellant's arguments of record and below, the following discussion summarizes the intended subject matter of the claims. This does not replace prior discussions of the claimed subject matter but is intended to present another description that may supplement and aid in understanding what is claimed.

As an aside, and as noted below in the discussion with respect to 35 U.S.C. §112, second paragraph, it is respectfully submitted that, if it would advance prosecution of this application, Appellant would consider amendment of the claims to render the intended subject matter more clear. The application and claims, however, are directed to methods in which the level of cell activation is used as a diagnostic indicator and as a point of therapeutic intervention.

As described in the application, Appellant has identified cell activation levels as a key parameter and indicator of risk of developing disease or as a point at which disease can be prevented or poor outcome mitigated (see, *e.g.*, Figure 2). The application describes and the claims encompass that finding that cell activation levels can serve in a way similar to other parameters that assess disease risk and also as a therapeutic point of intervention. This is discussed throughout the application and is depicted diagrammatically in Figure 2. In all claimed methods levels of cell activation are measured. These can be measured in individuals who are healthy or have a particular condition or disorder. Figure 2 exemplifies various states of a subject (or patient). For example, the subject can be healthy, or a pre-surgical patient, or can have symptoms of some disease or can have suffered traumatic injury. In all instances levels of cell activation are measured. The level of cell activation serves as diagnostic indicator and based upon the levels decisions of what course of action to pursue are made. The particular decision is related to the condition of the subject. For example, in healthy subjects the levels of cell activation can be used as a screening test. As described in the application, there are many known tests for measuring the level

of activation. Elevated levels of cell activation indicate that the subject has a risk of developing any or a number of disorders. To reduce the risk, cell activation lowering therapy can be initiated. The particular type of therapy is within the skill and judgment of the physician. For such subjects the risk of developing any of a variety of diseases is reduced, and perhaps disease is prevented. This embodiment and type of diagnostic/therapeutic test is analogous to other screening tests. For example, cholesterol levels are indicative of the risk of developing a variety of diseases, such as cardiovascular diseases and strokes. When one, for example, has a physical exam, cholesterol levels are measured. If elevated, therapy can be initiated. Therapy can involve administration of certain drugs or an alteration in diet or other therapy. The choice of therapy is within the skill and judgment of the treating physician. If such therapy is initiated and cholesterol is lowered, the treated subject may never have a heart attack or stroke. Hence, testing for cholesterol and initiation of therapy is a method for reducing the risk of developing disease and or can prevent disease. Similarly, testing the level of cell activation as claimed in the instant application prevent or reduce the risk of a disease.

Furthermore, using cholesterol levels as an example (cholesterol levels are not a measure of cell activation) of an analogous process, it would be nonsensical if a claimed method involving testing cholesterol levels, and, if elevated, administering therapy, were limited to a particular method of testing cholesterol and/or treating elevated cholesterol. Similarly, for the instantly claimed methods, it does not make sense to limit the method by which cell activation is measured to one particular test nor to limit the therapy that is initiated to one particular method. Cell activation testing methods and therapeutic methods are known to those of skill in the art and also are described in detail in the specification The instant application also provides a new method for reducing cell activation by administering a serine protease inhibitor, such as futhan. The claims, however, should not be limited to methods in which an element is limited to only the newly provided embodiment. The claimed

methods are generic methods that can be independent of a particular implementation.

Returning to Figure 2, in other embodiments, the subjects tested include pre-operative patients, patients with disorders, and trauma patients. For pre-surgical patients, elevated cell activation serves marker for risk of poor outcome of the patients. As claimed, lowering therapy can be initiated. As above, the particular therapy is within the judgment of the physician and the circumstances. Similarly, in trauma patients, elevated cell activation levels are indicative of a risk of poor outcome of treatment. In this case, the type of cell activation lowering therapy initiated will be dictated by exigent circumstances. Again such selection is within the skill and judgment of the physician. In all embodiments, however, the elements include the steps of testing for the level of cell activation, and if elevated initiating therapy prior to or with other therapies. As shown in Figure 2, initiation of cell activation therapy can reduce risks and/or prevent development of disease and/or aid in treatment decisions. The pending claims encompass these methods.

Claim 10 and dependents are directed to methods that include the steps of:

> assessing treatment options for a disease or condition by measuring cell activation levels in a subject with the disease or condition; and,
>
> if cell activation levels are elevated, administering activation lowering therapy prior to commencing treatment for the disease or condition, thereby improving treatment outcome or reducing risk of treatment.

Hence claim 10 encompasses embodiments in which the level of cell activation serves as an indicator of treatment outcomes in a subject, for example, with a disease or disorder or in a preoperative patient or a in a trauma situation.

Claim 32 and dependent claims are directed to a more general diagnostic/treatment method (analogous to diagnostic screening tests in which levels of metabolites or hormones or other biological effectors are measured). This

method is administered to anyone. The method includes:

> assessing cell activation in a subject; and, if elevated,
>
> administering activation lowering therapy, thereby preventing a disease or disorder or reducing the risk of a poor outcome of a treatment of a disease or disorder.

This method can be part of a routine screening or part of a treatment protocol. The level of cell activation is assessed. If it is high, then treatment to lower the cell activation level is initiated. One does not have to know what disease is being prevented or risk of poor outcome of treatment is being reduced. Just as one has one's cholesterol screened and therapy initiated if cholesterol levels are high, cell activation levels can be screened. Also as described in the specification, in a trauma or in surgical situations, it is observed that some patients survive and other seemingly similar patients do not. The application teaches that a difference between such patients is that the patients whose outcome is poor their level of cell activation is high. Hence, such method serves as guide for assessing treatment options.

Discussion and Rebuttal to the Examiner's Answer

(i) Claims 32-36, 38, 41, 42 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The Examiner continues to urge that there is there is no support for the phrase, "thereby preventing a disease" in the specification. The Examiner states:

> that specification does not give any evidence to support that the disease is prevented. No data or other evidence can be found that such diseases would be prevented in animal models or other models. Without such support, the claims are not enabled by the instant specification. To prevent a disease is to totally stop the disease from ever occurring. Appellant has not provided evidence that the disease is completely and utterly stopped and will never occur. In fact, there is no evidence on the record that such a method can even be practiced. There is no art on the record to state that such diseases/disorders can be prevented. How can one

> stop Alzheimer's from occurring? If one knew how to prevent an incurable disease such as Alzheimer's then the literature would be replete with such information which it is not.

The Examiner acknowledges that support for this preventing a disease or disorder is provided in the Appeal Brief, which references page 32, lines 10-17; page 137, line 25 to page 138, line 2; and page 144, line 20 of the specification to allegedly provide support for the language "thereby preventing a disease or disorder" in claim 32. The Examiner also states that "this the first time that appellant has shown this support in the specification."

This is not correct. First, such support has been referenced in numerous responses of record. For example, these pages and Example 8 were discussed in numerous responses of record, where this rejection was addressed For example, these pages and support are discussed in the responses mailed May 1, 2003 and October 14, 2003.

With respect to support, the Examiner urges that:

> [w]hile the support is noted, there is no evidence, *i. e.* data, that absolutely proves that any and all of the many different diseases or disorders under the sun can be prevented by using appellant's invention. Appellant points to a very specific example in the specification wherein rats were administered a pancreatic homogenate which supposedly puts the rats into shock. Appellant then claims that the rats dies if they were not administered the Futhan (the protease inhibitor)with the pancreatic homogenate. Appellant states that the rats recovered after a brief bout of hypotension. These results do not prove much. In fact, the rats could have died from the bout of hypertension that the futhan and the pancreatic homogenate put the rats through. In other words, it is not clear on the record that in every case a disease or disorder was prevented, in fact, in appellant's own specification appellant admits that this is not true since appellant states that the rat went through a bout of hypotension which is a disease or disorder which was not prevented. So, in fact, appellant has provided absolutely no conclusive evidence to support an extremely broad and unsupported claim set.

Appellant respectfully disagrees for the reasons of record. The claims recite "reducing the risk or preventing" this language cannot be ignored. As discussed above, "reducing the risk or preventing" does not mean every disease is prevented, only that following the steps of the method can reduce risk or can

prevent a disease from developing. The language of claim 32 and dependent claims, includes the step of assessing the level of cell activation; and, if elevated, initiating (or administering) cell activation therapy. The outcome (reducing risk or preventing a disease) is a consequence of performing the steps of the method. If one performs those steps, then, depending upon the subject, a risk of developing a disease or experiencing a poor outcome is reduced or the disease or poor outcome is prevent. There is no requirement that any and all diseases under the sun are prevented. The methods as claimed is directed to reducing the risk or preventing an outcome. Hence the claim does not require "prevention" but either reducing a risk or preventing an outcome. This is a therapeutic diagnostic method – like administering cholesterol lowering agents to prevent adverse consequences of high cholesterol – once does not know what disease has been prevented. To practice the method, one only has to perform the recited steps.

With respect to the specification and supporting evidence, the Examples provide a rodent model of disease. As described in the specification (see Example 3), hemorrhagic shock, which accompanies traumatic injury and is often fatal. The exemplified model well-known model of acute trauma. As described in the application, some victims of trauma survive and others victims who are of the same age and apparent health status (pre-trauma) die. The application shows that a difference between those who live and die is their level of cell activation. The rat model exemplified in Example 3 is a model that demonstrated that administration of cell activation lowering therapy *prevented death* (not shock). The results demonstrated that administration of cell activation lowering therapy can prevent an a poor outcome.

As claimed and described throughout the application, assessing the level of cell activation, serves as a diagnostic and therapeutic intervention point. First, it can be used for routine screening so that individuals can know and improve their status; and second, it also can be assessed when determining

courses of treatment to assess outcome of treatment and to improve the outcome of treatment.

Furthermore, the application describes in detail the relationship between activatied cells and various disease states and conditions. For example, in section B (see also Figure 1), the specification describes the relationship between cellular activation and disease in great detail. Section B describes various diseases and conditions and how and when to administer cell activation lowering therapy. Hence the application does establish that there is a link between cell activation levels and various diseases and the risks of development of diseases. It also teaches that reduction of levels of cell activation will reduce the risks of developing such diseases or prevent them or alter their outcome.

(ii) Claims 10-18, 32-36, 38, 41 and 42 are under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for treating hemorrhagic shock by assessing for free radical production using phenol red and then if levels are elevated using futhan, does not reasonably provide enablement for any and all activation lowering therapies and any and all diseases or conditions and any and all methods of assessing cellular activation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The Examiner makes a number of arguments, which are addressed in turn.

(a) The Examiner urges that:

> The specification as filed, is enabled for treating hemorrhagic shock by assessing for free radical production using phenol red and then if levels are elevated, using futhan, but is not enabled for any and all activation lowering therapies and any and all diseases or conditions and any and all methods of assessing cellular activation.
>
> The art of biotechnology is a highly unpredictable art and it would be an undue burden for one of ordinary skill in the art to test any and all activation lowering therapies and any and all diseases or conditions and any and all methods of assessing cellular activation to see if they could perform the claimed processes. With knowing only one activation lowering therapy,

> one condition to treat it with and only one type of assay in which to determine if it is necessary, one of ordinary skill in the art would not know what other conditions could be treated, what other therapies could be used or what other assays could be used to determine if such a method would work. Simply because such a method works with this combination does not mean that it will work for any and all combinations. The area of biotechnology is highly unpredictable since the human body in and of itself is very unpredictable.
>
> Applicant has only shown treating hemorrhagic shock by assessing for free radical production using phenol red and then if levels are elevated, using futhan. With only knowing this one combination of steps to yield the claimed method, it is clear that such broad claims are not enabled by the instant specification when one of ordinary skill in the art is only given this one combination.
>
> The state of the art is that there is no art. There is no guidance on which assay would be useful for which disease/condition. To know which assay to use for whatever disease ranging from a bruise to Alzheimer's is not known in the art, and thus no guidance for one of ordinary skill in the art which assay if any, would be effective to carry out the claimed method.

Appellant respectfully disagrees for reasons of record, which are summarized below. As discussed previously and above, the claims are directed to a method in which the level of cell activation is used as diagnostic indicator and point of therapeutic intervention. As discussed above, and exemplified in Figure 2, there are a variety of embodiments in which this method can be employed. The method is independent of the particular test by which the level of cell activation is assess and of the particular therapy that is initiated. As discussed previously, tests for cell activation are known to those of skill in the art and are discussed and described in detail in the specification. Therapies that will lower he level of cell activation are known and are outlined in the application.

For example, Figure 2 exemplifies the paradigm for the methods of assessing treatment options provided herein. Since activation is pivotal in disease outcomes, trauma outcomes, and general long term good health,

measurement of activation levels can be performed in healthy individuals who present no disorders. Identification of healthy individuals with elevated levels of activated cells, permits early identification of at-risk individuals and permits early intervention, in chronic and also in acute diseases. As shown in Figure 2, in a seemingly healthy patient activation levels are measured. If low, then no treatment or changes in lifestyle are recommended. If the levels are elevated, then tests to determine the presence of subclinical infection or other cell activating condition are performed. If those tests are negative, then lifestyle and diet should be examined, and if, necessary, modified. If diet is good, and lifestyle is generally good and stress-free, then activating lowering therapy can be instituted.

Testing cell activation levels pre-surgery, particularly elective surgery, then the levels can be used to assess the likely of complications from surgery and organ transplant rejection. If high levels of cell activation that are not the result of infection are found, then surgery should be postponed. Activation lowering therapy considered. Similarly, in unstable angina, the levels of cell activation are indicative of the risk of a cardiovascular event. Thus, if levels are high, activation lowering therapy and/or more aggressive treatment should be pursued. In trauma situations, the level of cell activation can aid in selecting treatment protocol and timing thereof. High levels of activation are associated with ARDS and MOF in the emergency room. Activation lowering therapy should reduce the risk thereof. Thus, in general, if a high level of cell activation is observed, then activation lowering therapy should be administered prior to further treatment.

The specification teaches that activation lowering therapy includes administration of known pharmaceuticals, such as aspirin and cardiovascular medications, dialysis and other such treatments. The application also describes a new method of lowering cell activation levels. The application shows that in addition to known methods for lowering cell activation, protease inhbitors, particularly serine proteases, exemplified by Futhan, can be administered

Section F, for example, of the application describes the therapeutic framework and teaches how to implement cell activation lowering therapy and parameters that guide choices. These include changes in diet and various drugs.

Hence it is incorrect that the application teaches only one method of measuring cell activation and one condition that can be treated and one treatment modality. The application describes and exemplifies a variety of tests and treatments. Treatment with a serine protease inhibitor is described because it is a new method, in addition to other treatments, such as aspirin therapy, exercise and diet, that lower levels of cell activation. Similarly, there are numerous methods known to assess cell activation. The instantly claimed methods are directed to a new use for these therapies and testing methods.

(b) The Examiner continues:

> Concerning the second 35 U.S.C. §112, first paragraph rejection, appellant has argued that the examples in the specification allegedly provide one of the ordinary skill in the art with enough information so that one of the ordinary skill in the art can figure out how to make and use the other many possibilities of the invention.
>
> While this is very interesting on its face, when one actually looks at the claims one can see that the claims encompass alterations in one's lifestyle to reducing stress as a means of "activation lowering therapy" which reads on taking a day off from work. This is a completely different type of "activation lowering therapy" to dialysis. Why would one of ordinary skill in the art think that if one can take a day off from work that that would also mean that that dialysis would also be effective in practicing this method.

Appellant respectfully disagrees. As discussed above, the particular therapy initiated is within the level of skill of the physician and is in part dictated by the subject tested. As discussed for healthy individuals who are being screened for the level of cell activation, a change in lifestyle or a reduction in stress may be selected and effective. For a trauma patient treatment will be required to more immediate and fast acting For pre-surgical patients, less immediate therapies can be selected.

(c) The Examiner continues:

> Further, the invention is broadly claimed in its claiming of the "disease or condition". The disease or condition can range from trauma (which is vague and broad in and of itself) to stroke. Why would one of ordinary skill in the art think if the method can be used to treat trauma which encompasses a bruise to treating Alzheimer's? There is simply no correlation between the allegedly "closely related" species that appellant is claiming.

The Examiner is correct that the disease or condition can range from trauma to stroke to Alzheimer's Disease. The method, however, targets and assesses the level of cell activation and it is the level of cell activation that is treated and that affects a subject's response to a bruise or a risk of developing Alzheimer's or other diseases. The particular disease or condition is not treated. As discussed above and throughout the prosecution history of this application, the nexus among these conditions and diseases is the level of cell activation, which serves as a diagnostic indicator. Hence, if one has a high level of cell activation their response to a trauma will be exacerbated and the risk of developing - It is not the bruise or Alzheimer's that is being treated, but the level of cell activation that can, if elevated, exacerbate or lead to a poor outcome or increased risk of developing a disease

(d) The Examiner continues:

> Finally appellant is claiming a very broadly defined, "assessing treatment options for a disease or condition by measuring cell activation levels in a subject ". This reads on just about anything as well. Even if one of ordinary skill in the art did envision one particular type of assay for assessing cell activation levels in a patient as argued by appellants on page 29 of the brief, one of ordinary skill in the art would not know which assay to use to measure such levels for a person who has a bruise versus someone who has Alzheimer's. The two conditions/diseases are completely unrelated and share no commonality in any way. Thus, to come to some common assay or know which assays could be used for either is simply not known. If one knows that a particular assay is useful to detect low activation cell levels in a person who has Alzheimer's how can one of ordinary skill in the art know from that which assay might be of assistance to him in finding out which activation cells levels might be elevated in a person who has a bruise totally unrelated to Alzheimer's. They are completely different disease/disorders and such share no commonalities at all.

Again, Appellant respectfully disagrees. The fact that the conditions/diseases do not share symptoms is not relevant. The parameter that is measured is the level of cell activation. The level of cell activation can be measured by any suitable assay therefor. It is a matter of taking a blood sample and assessing the level of cellular activation. The disease or health status of the patient does not affect the test that is employed. The test assesses the level of activated cells, not the particular disease or condition. The treatment option that is assessed is whether or not to initiate or administer cell activation lowering therapy and the risk to a patient of treatment, such as elective surgery, for their condition. If cell activation levels are high, then, the physician may opt for a less invasive treatment.

(e) The Examiner continues:

> The state of the art is that there is no art. There is no guidance on which assay would be useful for which disease/condition. Appellant tries to offer the argument that one of ordinary skill in the art would really know which assay to use for whatever disease ranging from a bruise to Alzheimer's but the fact of the matter is that there is no art, and thus no guidance for one of ordinary skill in the art which assay if any, would be effective to carry out the claimed method.

As discussed above and in the record, the parameter measure, cell activation, is the same. Any test that measure the level of cell activation can be selected; the test is independent of the subject/patient's health status.

(iii) The rejection under 35 U.S.C. § 112, second paragraph.

Claims 10-18, 32-36, 38, 41 42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Appellant regards as the invention. Appellant continues to traverse this rejection. The omission of the word "cell" before "activation lowering therapy" is acknowledged. If needed to render the claim more clear, the claim can be amended by insertion of the word "cell" before activation. The Examiner states:

> Appellant argues that the 35 U.S.C. §112, second paragraph rejection is allegedly in error since appellant believes that one of ordinary skill in the art would know what "administering activation lowering therapy" means. Fact is, since the term has such a broad meaning as is evidenced by the appellants themselves in their broad definition of the term on page 19 of the specification,

> how can one of ordinary skill in the art know what it really encompasses since it reads on everything from taking a day off from work to taking futhan. A lifestyle change could also read on moving to Hawaii or becoming a monk. Is that really what the invention is? This term is confusing an appellant has not amended it to make the true meaning of the term clear.

Appellant respectfully disagrees. The omission of the word "cell" before "activation lowering therapy, " however, is acknowledged. If needed to render the claim more clear, the claim can be amended by insertion of the word "cell" before activation. As discussed above, the claim recites "preventing a disease or disorder." Appellant refers the examiner to the argument above with regard to the discussion of this language with respect to 35 U.S.C. §112, first paragraph rejection. The steps of the method do not require that one affirmatively prevent anything. The methods involve assessing the level of cell activation and then if elevated administering cell activation lowering therapy. The prevention or reduction in risk or is the outcome of following the steps of the method.

Furthermore, the meaning will be understood one of skill in the art. As discussed above, with respect to cholesterol screening, those of skill in the art would understand that if one lowers ones cholesterol certain diseases can be prevented. Similarly, with respect to the instantly claimed methods, one of skill in the art would understand that lowering levels of cell activation can result in prevention of a disease. he claimed methods constitute methods of diagnostic and therapeutic intervention. Just as one has one cholesterol tested and then if it is elevated, takes cholesterol lowering agents to reduce the risk or prevent cardiovascular disease, the instantly claimed methods are intended as a diagnostic test and therapeutic intervention that results in reducing the risk of developing a disease or preventing a disease from developing or manifesting. Using the analogy discussed above, one takes cholesterol lowering agents to prevent cardiovascular disease. Until the individual dies, one would never know whether the disease was completely prevented. Those of skill in the art understand that lowering cholesterol can reduce the risk of developing cardiovascular disease or can prevent development of the cardiovascular disease. The language of the instant claims is intended to be

analogous. One tests the level of cell activation, if the level of cell activation is high, one initiates treatment to reduce the level. The application teaches that the level of cell activation is associated with the risk of developing a variety of diseases. If the level of cell activation is reduced, then the risk of developing such diseases is reduced and a disease may be prevented. The claim recites "reducing the risk or preventing." Performing the steps of the methods as claimed results in "reducing the risk or preventing."

The Examiner also urges that "[i]t is not clear what is meant by "administering activation lowering therapy". He asks whether a " method or a compound" is administered. As noted throughout the prosecution history of this application and as defined in the application activation lowering therapy constitutes any methods, including administration of therapeutics, lifestyle changes, dietary changes, that result in lowering the level of cell activation. Appellant is not adverse to selecting or employing different word than "administering." Words such as "initiating" or "commencing" cell activation lowering therapy are suitable substitutes.

Whatever language employed, the specification clearly describes and teaches what is meant by cell activation lowering therapy. For example, at page 19, the specification states:

> As used herein, activation lowering therapy (A.L.T.) refers to any means in which the level of activated cells is lowered. Such means include lifestyle and dietary changes, drug therapy, such as aspirin, pentoxifylline, Daflon 500 (a flavenoid), anti-inflammatories, inderal, heparin, coumadin, Futhan and other protease inhibitors

Thus, cell activation lowering therapy refers to any therapeutic regimen that results in lowered levels of activated cells. As stated in the application, methods for lowering cell activation are well known to those of skill in the art. It is within the skill of the treating physician to select a method suitable for the circumstances. The specification outlines various exemplary circumstances. For example, Figure 2 exemplifies a number of circumstances and suitable cell activation lowering treatments.

* * *

In view of the above arguments and the arguments of record in the file history of the application, favorable consideration and allowance of the appealed claims are respectfully requested.

Respectfully submitted,

By: _____
Stephanie Seidman
Registration No. 33, 779

Attorney Docket No. 17124-003001/2202
Address all correspondence to:
Stephanie Seidman
FISH & RICHARDSON P.C.
1230 El Camino Real
San Diego, California 92130
Telephone: 858 678-4777
Facsimile: 202-626-7796
email:seidman@FR.com

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P.O. Box 1450
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TRANSMITTAL LETTER

Dear Sir:

Transmitted herewith are a Reply Brief, and a check to preserve the right to an oral hearing. If needed this letter constitutes a request for an oral hearing.

Any fees that may be due in connection with this paper or with this application during its entire pendency to Deposit Account No. 06-1050. A duplicate of this sheet is enclosed.

Respectfully submitted,

Stephanie Seidman
Registration No. 33,779

Attorney Docket No. 17106-027001 / 1616
Address all correspondence to:
Fish & Richardson P.C.
12390 El Camino Real
San Diego, California 92130
Telephone: (858) 678-5070
Facsimile: (202) 626-7796